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14. ABSTRACT Fragile X (FX) syndrome causes behavioral disturbances such as labile mood, anxiety, hyperactivity, and aberrant behavioral responses to stress. Affected males may suffer from learning disabilities, attention deficit disorders, mental retardation, or autism spectrum disorders. We seek to address the most effective methods of treatment (pharmacological and behavioral) for the symptoms and behavioral problems associated with FX syndrome. During the past year, we have established a comprehensive FX syndrome clinic and we continue to refine our treatment protocol. Collaborative relationships have been established with genetics, speech/language, psychiatry, and dental so that families can obtain these services from specific professionals with an interest in FX syndrome. School liaison services for school aged youth with FX syndrome have been established. Community education programs, in the form of a website, a parent advisory group, and announcements have been established. We continue to refine our database to track the frequency of the disease and specific symptoms with the goal of guiding future treatment through evidence based medicine.					
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Pharmacological and Nonpharmacological Methods of Treatment of
Fragile X Syndrome
02/01/05 – 01/31/06

INTRODUCTION:

The Child Development Unit, Center for Neurosciences, and Division of Genetics of the Children's Hospital of Pittsburgh (CHP) are seeking to address the most effective methods of treatment – both pharmacological and non-pharmacological -- for the symptoms and behavioral problems associated with Fragile X (FX) syndrome.

This program will feature the recruitment of children with this disorder to conduct physiological and behavioral testing, with the goal of identifying effective interventions.

A local established registry will supply data on the behavioral phenotype of children with FX syndrome for future basic and clinical research as well as establishing best practice models for clinical care.

This problem will establish a basic research program including development of genetically engineered mouse and primate models of the syndrome to determine the mechanism of, and potential novel treatments for symptoms of FX syndrome.

STATEMENT OF HYPOTHESIS

FX syndrome causes behavioral disturbances such as labile mood, anxiety states, hyperactivity, and aberrant behavioral responses to stress. Affected males may suffer learning disabilities, attention deficit disorders, mental retardation, and autism spectrum disorder. The Child Development Unit, Center for Neurosciences, and Division of Genetics at the Children's Hospital of Pittsburgh (CHP) now seek to address the most effective methods of treatment – both pharmacological and non-pharmacological – for optimal management of the symptoms and behavioral problems associated with FX syndrome. This initiative features the recruitment of children with this disorder to conduct physiological and behavioral testing, with the goal of identifying effective interventions. Finally, this initiative will establish a basic research program including development of genetically engineered mouse and primate models of the syndrome to determine the mechanism of, and potential novel treatments for symptoms of FX syndrome. Because the behavioral symptoms occurring in youth with FX syndrome also occur commonly in non-FX subjects and may affect the behavioral responses to stressful conditions, the overall program will have an impact on military personnel as well as children and families affected by FX syndrome.

OBJECTIVES

1. To establish a clinical center for diagnosis and treatment of individuals with FX syndrome
2. Provide community service and professional education about FX syndrome
3. To develop a registry for FX patients and their families

4. To establish a basic research laboratory dedicated to studies on the pathobiology of neurobehavioral disturbances in FX syndrome, with a particular focus on new genetically engineered animal models of the syndrome

ACCOMPLISHMENTS (Year 2/1/05 – 1/31/06)

Objective 1: To establish a clinical center for diagnosis and treatment of individuals with FX syndrome

- Dr. Robert Noll and Rebecca Kronk have established a monthly Fragile X Center clinic. We are currently seeing all patients in the region with FX syndrome, full and pre-mutation, and their families for comprehensive care visits.
- Dr. Dena Hofkosh serves as clinical medical consultant and is available as needed during the monthly Fragile X Center session.
- We are increasing the number of children being referred to the Center through continued outreach efforts towards primary care physicians in the tri-state area.
 - Dr. Randi Hagerman's Grand Rounds in December, 2005, has been archived and made accessible on the Children's Hospital Fragile X Website for professionals as well as families locally, regionally, and nationally.
 - We have developed a brochure (reviewed by Michael Tranfaglia, MD, Medical Director of FRAXA Research Foundation, parent representatives, and CHP Public and Government Affairs) for distribution to community members involved in the coordination of care of children with FX syndrome. The purpose of the brochure is to increase awareness of the incidence of FX syndrome. This brochure is also appropriate for parents, schools, and other community agencies involved with children who may be at risk for FX syndrome.
 - Phone calls, approximately one dozen per month, coming to the Center from individual providers and families, regarding appropriate diagnostic testing and referrals are being promptly addressed by the coordinator of the Fragile X Center.
 - In collaboration with CHP Public and Government Affairs, we have developed the CHP FX Center website http://www.chp.edu/clinical/03a_fragilex.php. This website provides access to information about the Center and provides links to other local and national resources.
 - In response to the positive feedback from families who have been given our Fragile X CHP Parent Handbook as well other medical providers, an e-version has been made available on the CHP Fragile X Center website. The result of this should allow for greater access and dissemination of information about Fragile X.
 - In January 2006, Dr. Robert Noll spoke to CCP about the Fragile X Center and available services.

- Dr. Robert Noll and Rebecca Kronk, CRNP have continued to establish relationships and communication with the National Fragile X Foundation, FRAXA Research, the MIND Institute, and the University of NC Durham Fragile X Center. The FX Foundation featured an announcement about the FX Center at CHP in September, 2005. Persons calling the National FX Foundation to find resources in Western Pennsylvania or the surrounding areas are provided information about the CHP Fragile X Center.
- Our multi disciplinary provider network representing Genetics, Ophthalmology, Dental, and Psychiatry, has been in place for one year. This group, comprised of dedicated specialists, both within CHP and UPMC, is committed to providing improved access to appropriate and necessary healthcare follow up for Fragile X patients. This provider network has offered a professional, efficient and seamless approach to referrals for patients seen in the Center.
- We have established a community education program for FX syndrome. FX clinic interdisciplinary team members provide information to the quarterly newsletter about research, tips on behavioral management, and information about upcoming educational events such as web casts. A set of educational materials, donated to the FX clinic at CHP by the National FX Foundation, forms the foundation for our developing lending library. This library is available to FX clinic interdisciplinary team members and families of children seen in the clinic.

Objective 2: Provide community service and professional education about FX syndrome

- Dr. Noll and Rebecca Kronk attended the 9th National FX Conference. Extensive networking has resulted in a solid working relationship with individuals at the local, state, and national level. In the forthcoming year, Fragile X Center staff will attend at least 5 additional events or meetings that will afford them further opportunity to build on relationships with colleagues in the Fragile X community.
- Locally -- Two meetings have been held with parents of children with FX syndrome to discuss how the FX Center might better address the needs and concerns they have for their children. The group decided to form a parent advisory group to work collaboratively with the staff of the FX Center and the ancillary interdisciplinary team members of the Center.
- State -- Dr. Noll has established contact with Mr. William Parker in Harrisburg. The Parkers (William and Debra) are interested in establishing a parent support network in Pennsylvania as well as securing funding sources for FX clinical services. Dr. Noll has been working with this family to facilitate their goals and ensure that the CHP clinic is providing necessary support.
- Nationally -- A meeting facilitated by the local parent advisory group, was held at the Child Development Unit with Dr. Michael Tranfaglia, Medical Director of FRAXA Research Foundation. Dr. Tranfaglia offered the support of FRAXA as well as his own support of the establishment of the clinic. Staff from the Fragile X Center met with Dr.

Randi Hagerman resulting in an invitation to the MIND Institute and an offer to collaborate further in joint research endeavors.

- Goals for next year:
 - We have developed a primary care physician packet of information which will include the CHP FX clinic brochure; information about the recommended lab protocol for diagnostic testing when there is a suspicion of FX syndrome; and the American Academy of Pediatric Practice Guidelines of Care for patients with FX syndrome. This packet will be distributed by CHP Public and Government Affairs regionally to 3500 primary care physicians. The purpose will be to increase awareness of the primary care physician of the frequency and incidence of FX syndrome within their practice; inform them about current updates on FX syndrome; and provide information about services offered to families through our center and the collaborating interdisciplinary team members.
 - Visit the MIND Institute, participate in the National Fragile X Advocacy Day in Washington, and attend the International Fragile X Conference in Atlanta. Continue efforts to focus on keeping colleagues in the Fragile X Community informed about the FX Center at CHP.
 - A regional FX syndrome conference is being planned for an audience of parents and professionals involved in the health care of patients with FX syndrome. We are hopeful that Dr. Michael Tranfaglia, Medical Director of FRAXA Research Foundation, will be available as our keynote speaker.
 - Maintain our solid working relationship between our parent advisory group and the Fragile X Center staff. We will have 2 meetings this year.
 - The biennial gala (the X Ball) will be held May 11, 2006, in Pittsburgh in celebration of the opening of the CHP Fragile X Center. This event will benefit FRAXA Fragile X Research Foundation and the CHP Fragile X Center. We anticipate guests from throughout the nation.

Objective 3: To develop a patient registry and data base for FX syndrome patients and their families.

- Approval has been obtained from the University of Pittsburgh IRB for the establishment of a patient registry for patients with Fragile X. Thus far, 4 families have been approached during clinic visits and all have consented to become eligible.
- We are working with the manager of Applications and Integration at CHP to build a clinical database that will provide the framework to collect developmental, demographic, medical, and behavioral information on our population of children seen through the Fragile X Center.
- Goals for next year:
 - Utilize Research Assistant/Graduate Student to obtain developmental, psychometric, and behavioral data from Fragile X patients and their families.
 - To facilitate inclusion of our families in ongoing clinical research programs for individuals with FX syndrome. This would be made possible by increases in the number of individuals with FX syndrome served by the clinic.

- To disseminate information about existing research studies, endorsed, and supported, in progress at other institutions to increase the fund of knowledge about FX syndrome.

Objective 4: To establish a basic science research laboratory.

- A search committee of Dr. Perlmutter, PI, Chair of Pediatrics, Dr. Robert Noll, Chief of Child Development Unit, Dr. Jerry Vockley, Chief of Genetics, Dr. Nina Schor, Chief of Neurology, and Dr. Ron Dahl, WPIC, continues its search for a senior scientist.

REPORTABLE OUTCOMES

There have been no publications in referred journals or grant applications this year.

A website has been established and a Children's Hospital of Pittsburgh brochure for Fragile X has been developed.

CONCLUSIONS

The CHP FX syndrome center is continuing to emerge as an entity gaining recognition locally and nationally while addressing the needs of families and children with a diagnosis of FX syndrome.